REMARKS

Claims 1-4 are pending in the instant application.

I. The Amendments

Claims 5-10 are canceled as being drawn to a non-elected invention. Claim 1 has been amended for the purpose of clearly defining what Applicants consider to be the invention. Specifically, the claim has been amended for grammatical consistency and clarity. This amendment does not raise new issues, does not introduce new matter, and it is fully supported by the specification and Claim 1 as originally filed. Therefore, entry under 37 C.F.R. § 1.116 is respectfully requested.

A marked-up version of the amended claims is attached hereto as *Appendix A*. The claims as presently pending are attached hereto as *Appendix B*.

II. Allowable Subject Matter

The Applicants note with appreciation that Claim 4 is allowable.

III. The Rejections

A. Rejection of Claims 1 And 2 Over Evans And The '834 Patent Under 35 U.S.C. § 103(a)

Claims 1 and 2 are rejected under 35 U.S.C. § 103 as being obvious over Evans *et al.*, 1992, *Journal of Immunological Methods* 156:231-238 ("Evans") of record, in view of U.S. Patent No. 5,840,834 (the "'834 patent"), newly cited. This rejection is respectfully traversed.

In order to make a *prima facie* showing of obviousness, the Examiner bears the initial burden of citing a combination of references that, *inter alia*, teaches each and every element of the claimed invention. *See In re Vaeck*, 20 USPQ2d 1438 (Fed. Cir. 1991). The Examiner must show that the cited references teach or suggest the claimed invention, and that, at the time of the invention, the skilled artisan would have had a reasonable expectation of success that the claimed invention would work. Further, the Examiner cannot, in hindsight, combine references unless the references provide a motivation to do so, and he has to consider the teachings provided by the references as a whole. Applicants submit that the Examiner has failed to meet his burden of establishing a *prima facie* case of obviousness.

The present invention is directed to an antibody against the histidine portion of a fusion polypeptide. The histidine portion of the fusion polypeptide is specified to comprise 6-18 successive histidine residues.

Evans teaches, as characterized by the Examiner, the making of polyclonal antibodies directed to fusion proteins containing metal binding peptides, wherein the antibodies are made against a metal binding peptide that comprises three histidine residues. The Examiner further states that Evans also teaches that the antibodies are useful in detecting fusion proteins containing metal-binding peptides that have been purified by immobilized metal affinity chromatography. The Examiner, however, concedes that Evans ***does not teach antibodies*** which ***bind a metal binding protein containing six to eighteen consecutive histidine residues***.

The Examiner asserts that this shortcoming is filled in by the '834 patent. According to the Examiner's characterization, the '834 patent teaches fusion proteins containing six

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consecutive histidine residue metal binding peptides, wherein the fusion proteins are purified using an organic chelator designated CM-Lys linked to a peroxidase enzyme. Applicants respectfully disagree that the teaching of the '834 patent provides the missing elements of Evans.

The Combination of Cited References Does Not Teach or Suggest the Claimed Invention. In accordance with the Examiner's own statements, Evans fails to teach antibodies which bind a histidine portion of a fusion protein, where the histidine portion comprises six to eighteen ***consecutive*** histidine residues. The Examiner asserts that the '834 patent fills in this missing piece. However, this assertion is not well taken. Applicants respectfully point out that the '834 patent is not directed to any type of antibodies, let alone antibodies binding the histidine portion of a fusion protein. Accordingly, the '834 patent cannot provide for the missing piece of Evans, -- an antibody that binds a histidine portion comprising six to eighteen consecutive histidine residues. Thus, the combination of Evans and the '834 patent does not teach all the elements of the claimed invention, as required by the law for the advancement of a *prima facie* case of obviousness. Therefore, the rejection of Claims 1 and 2 under 35 U.S.C. § 103(a) as being over Evans in view of the '834 patent is in error and should be withdrawn.

The Skilled Artisan Would Not Have Been Motivated to Combine the Cited References. The Examiner asserts that one skilled in the art at the time the invention was made would have been motivated to substitute the six histidine metal binding peptide taught by the '834 patent for the three histidine metal binding peptide taught by Evans, "because Evans teaches antibodies to metal binding peptides are useful to detect fusion proteins

containing said metal-binding peptides purified by IMAC." *See*, Office Action, at page 3. Applicants respectfully disagree that the references contain motivation to combine their teaching. Evans is interested in ***immunological detection of a metal binding peptide*** that happens to include three non-consecutive histidine residues (*His-Asp-His-Asp-His*). The '834 patent, in contrast, uses a histidine tag for the detection of fusion proteins using ***non-immunological*** detection methods, namely the organic chelator CM-Lys linked to a peroxidase enzyme. Nothing in the cited references provides motivation to make antibodies against the histidine tag provided by the '834 patent. The teaching of Evans that one can make antibodies against a *His-Asp-His-Asp-His* peptide is completely unrelated to the making of antibodies against a histidine portion comprising between about six and about eighteen ***consecutive*** histidine residues. Accordingly, the cited references do not provide a motivation to combine the teachings set forth therein. Thus, the combination of references advanced by the Examiner is improper, and the rejection of Claims 1 and 2 under 35 U.S.C. § 103(a) should be withdrawn.

B. Rejection of Claim 3 over Evans, in View of the '834 Patent and Sevier under 35 U.S.C. § 103(a)

Claim 3 is rejected under 35 U.S.C. § 103(a) as being obvious over Evans, in view of the '834 patent and further in view of Sevier *et al.*, 1981, *Clinical Chemistry* 27:1797-1806 ("Sevier").

The Examiner states that the claimed invention in Claim 3 differs from the prior art teachings only by the recitation of a monoclonal antibody which binds the histidine tagged fusion protein. He asserts that Sevier fills in this shortcoming. Specifically, according

to the Examiner, Sevier teaches the making of monoclonal antibodies from known antigens, referring to page 1797, column 2, and that monoclonal antibodies are more homogenous, specific and more easily available than polyclonal antibodies.

Applicants submit that the combination of the Evans, the '834 patent and Sevier in support of the rejection of Claim 3 fails for the same reason as the rejection of Claims 1 and 2 over Evans and the '834 patent. Accordingly, the rejection of Claim 3 under 35 U.S.C. § 103(a) over Evans, the '834 patent and Sevier should be withdrawn.

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CONCLUSION

In view of the above remarks, the subject application is believed to be in good and proper order for allowance. Early notification to this effect is earnestly solicited.

If, in the opinion of the Examiner, a telephone conference would expedite the prosecution of the subject application, the Examiner is encouraged to call the undersigned at (650) 493-4935. The commissioner is authorized to charge any underpayment or credit any overpayment to Deposit Account No. 16-1150 for any matter in connection with this response, including any fee for extension of time, which may be required.

Respectfully submitted,

Date December 14, 2001

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Enclosure

APPENDIX A
United Sates Application Serial No. 09/485,793
Marked-Up Versions of Amended Claims
(Additions are underlined; Deletions are bracketed)

1. (Thrice amended) An antibody against a fusion polypeptide, wherein said fusion polypeptide comprises a histidine portion, wherein said antibody is directed against said histidine portion, and wherein said histidine portion comprises 6-18 successive histidine residues.

2. (Reiterated) The antibody of Claim 1, wherein said antibody is a polyclonal antibody.

3. (Reiterated) The antibody of Claim 1, wherein said antibody is a monoclonal antibody.

4. (Reiterated) An antibody, wherein said antibody is deposited under ACC 2207 with the Deutsche Sammlung von Mikroorganismen und Zellkulturen GmbH (DSM).

5. (Cancel)

6. (Cancel)

7. (Cancel)

8. (Cancel)

9. (Cancel)

10. (Cancel)